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EXAMINER	
LAMM, MARINA	

ART UNIT	PAPER NUMBER
1616	32

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/500,115	PONIKAU, JENS	
	Examiner	Art Unit	
	Marina Lamm	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *70-120,122,123,127-129,135-137,143-145 and 194-243* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *70-120,122,123,127-129,135-137,143-145 and 194-243* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The application has been withdrawn from issue due to unpatentability of one or more claims. See Notice dated 6/30/03 (paper #31).

2. Claims pending are 70-120, 122, 123, 127-129, 135-137, 143-145 and 194-243.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 70 and 122 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing asthma and non-invasive fungus-induced rhinosinusitis, does not reasonably provide enablement for eliminating said conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same..." The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni,

195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). They include: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or unpredictability of the art, (4) the relative skill of those in the art, (5) the breadth of the claims, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the claimed invention without undue experimentation.

(1) the nature of the invention

The invention provides a method for treating a mammal having asthma and non-invasive fungus-induced rhinosinusitis, comprising mucoadministering to said mammal a formulation in an amount, at a frequency, and for a duration effective to reduce or eliminate said asthma and said non-invasive fungus-induced rhinosinusitis, said formulation comprising an antifungal agent. The Concise Oxford Dictionary defines the term "eliminate" as "completely remove or get rid of". See Concise Oxford Dictionary 10th Edition, 1999.

Therefore, the limitation "effective to...eliminate said asthma and said non-invasive fungus-induced rhinosinusitis" reads on *curing* said asthma and said rhinosinusitis.

(2) the state of the prior art

The prior art teaches combating recurrence of allergic fungal sinusitis (AFS) by topical application of antifungal agents. See Bent III et al., "Antifungal Activity Against Allergic Fungal Sinusitis Organisms", Laryngoscope, 106, 1996, pp. 1331-1334, supplied by the Applicant. However, Bent III et al. teach that "[s]ince the topical antifungals would not change the underlying AFS immunopathology, they should not be regarded as potentially curative, but simply a useful adjunct to current standard therapy." See p. 1333. With respect to asthma, the methods of preventing and controlling asthma symptoms, reducing the frequency and severity of asthma exacerbation and reversing acute airflow obstruction are well known in the art; the common therapy includes steroids, $beta_2$-agonists and anti-inflammatory medications. See "Guidelines for the Diagnosis and Management of Asthma", July 1997, pp. 59-123, supplied by the Applicant. Jain et al. teach that currently there is no hope of a cure for allergic asthma. See Jain et al., "CpG DNA and immunotherapy of allergic airway diseases", Clinical and Experimental Allergy, 33 (10), 1330-5, Oct. 2003, Abstract. Allergen avoidance and immunotherapy seem to be the only hopes for significantly improving asthma for those patients who have an allergic component to their disease. See Kaliner, "Goals for asthma therapy", Annals of Allergy, Asthma, and Immunology, 75(2), 169-172, Aug. 1995, Abstract. However, Guidelines for the Diagnosis and Management of Asthma regard allergen avoidance and immunotherapy as a part of asthma management, rather than "cure". See pp. 41-49.

While teaching treating (managing) asthma symptoms and fungus-induced rhinosinusitis, the prior art does not teach *curing or eliminating* the diseases by administration of antifungal agents. On the contrary, prior art suggests that there is currently no cure (except for, perhaps, allergen avoidance) for asthma and/or fungus-induced rhinosinusitis. See above.

(3) the predictability or unpredictability of the art

The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. See MPEP 2164.03. In this case, the prior art lacks knowledge in regards to the curing or eliminating asthma and/or fungus-induced rhinosinusitis by administration of antifungal agents. Presently, there is no medical cure for the diseases. At best, the prior art teaches methods of preventing and controlling asthma symptoms and combating recurrence of allergic fungal sinusitis. See above. Further, the Court in *In re Fisher* stated that physiological activity is an unpredictable factor. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). Thus, the unpredictability of the art is high.

(4) the relative skill of those in the art

The relative skill of the those in the art is high.

(5) the breadth of the claims

The claims are very broad. They encompass treating asthma and non-invasive fungus-induced rhinosinusitis with *any* antifungal agent.

(6) the amount or direction or guidance presented

The instant specification discloses a method of treating asthma and rhinosinusitis caused by non-invasive fungal organisms. Thus, the specification is enabling for such method. The specification does not provide sufficient guidance to allow one skilled in the art to use the claimed method for *curing or eliminating* of asthma and AFS. There is insufficient guidance and objective evidence in the art that would indicate that antifungal agents (or any chemical agents) will be able to cure asthma and AFS. The fact that antifungal agents nystatin and amphotericin B were demonstrated to be somewhat effective agents for the treatment of asthma and AFS, is not an evidence that they will be effective in curing or elimination of those conditions. As stated above, the prior art currently does not recognize the possibility of curing either condition by pharmacological therapy.

(7) the presence or absence of working examples

The examples in the specification are directed to the treatment of said conditions rather than the claimed elimination. The specification does not provide any working examples that would indicate the claimed antifungal agents are capable of completely eliminating asthma and AFS.

(8) the quantity of experimentation necessary

The specification provides insufficient guidance with regard to the claimed method and contains no working examples and no evidence which would allow one of skill in the art to

predict the efficacy of the claimed method of curing with a reasonable expectation of success. Moreover, the nature of the invention and the state of prior art have not provided any reasonable expectation of success in curing of asthma and AFS. For the above reasons, it appears that one skilled in the art could not practice the invention with the claimed breadth without an undue amount of experimentation.

Therefore, the instant specification does not provide enablement commensurate with the scope of the claim.

5. Claims 119, 120, 242 and 243 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating asthma and/or non-invasive fungus-induced rhinosinusitis, does not reasonably provide enablement for preventing/prophylaxis of said conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

As stated above, factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, include: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or unpredictability of the art, (4) the relative skill of those in the art, (5) the breadth of the claims, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the claimed invention without undue experimentation.

(1) the nature of the invention

The invention provides a method for treating a mammal having asthma and non-invasive fungus-induced rhinosinusitis, comprising mucoadministering to said mammal a formulation comprising an antifungal agent and after said mucoadministration, prophylactically mucoadministering to said mammal a prophylactic formulation in an amount, at a frequency, and for a duration effective to prevent said asthma or said non-invasive fungus-induced rhinosinusitis, said prophylactic formulation comprising an antifungal agent.

(2) the state of the prior art

The prior art teaches combating recurrence of allergic fungal sinusitis (AFS) by topical application of antifungal agents. See Bent III et al., "Antifungal Activity Against Allergic Fungal Sinusitis Organisms", Laryngoscope, 106, 1996, pp. 1331-1334, supplied by the Applicant. With respect to asthma, the methods of preventing and controlling asthma symptoms, reducing the frequency and severity of asthma exacerbation and reversing acute airflow obstruction are well known in the art; the common therapy includes steroids, $beta_2$-agonists and anti-inflammatory medications. See "Guidelines for the Diagnosis and Management of Asthma", pp. 59-123, supplied by the Applicant. However, the art teaches preventing the asthma symptoms, rather than the disease itself. While teaching treating (managing) asthma symptoms and combating recurrence of fungus-induced rhinosinusitis, the prior art does not teach *preventing* the diseases by administration of antifungal agents.

(3) the predictability or unpredictability of the art

The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed

invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. See MPEP 2164.03. In this case, the prior art lacks knowledge in regards to the preventing asthma and/or fungus-induced rhinosinusitis by administration of antifungal agents. At best, the prior art teaches methods of preventing and controlling *asthma symptoms* and combating *recurrence* of allergic fungal sinusitis. See above. Further, the Court in *In re Fisher* stated that physiological activity is an unpredictable factor. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). Thus, the unpredictability of the art is high.

(4) the relative skill of those in the art

The relative skill of the those in the art is high.

(5) the breadth of the claims

The claims are very broad. They encompass preventing asthma and non-invasive fungus-induced rhinosinusitis with *any* antifungal agent.

(6) the amount or direction or guidance presented

The instant specification discloses a method of treating asthma and rhinosinusitis caused by non-invasive fungal organisms. Thus, the specification is enabling for such method. The specification does not provide sufficient guidance to allow one skilled in the art to use the claimed method for *preventing* asthma and AFS. There is insufficient guidance and objective evidence in the art that would indicate that antifungal agents (or any chemical agents) will be

able to prevent asthma and AFS. The fact that antifungal agents nystatin and amphotericin B were demonstrated to be somewhat effective agents for the treatment of asthma and AFS, is not an evidence that they will be effective in preventing of those conditions.

(7) the presence or absence of working examples

The examples in the specification are directed to the treatment of said conditions rather than the claimed prevention. The specification does not provide any working examples that would indicate the claimed antifungal agents are capable of preventing asthma.

(8) the quantity of experimentation necessary

The specification provides insufficient guidance with regard to the claimed method and contains no working examples and no evidence which would allow one of skill in the art to predict the efficacy of the claimed method of preventing with a reasonable expectation of success. Moreover, the nature of the invention and the state of prior art have not provided any reasonable expectation of success in preventing asthma and AFS. For the above reasons, it appears that one skilled in the art could not practice the invention with the claimed breadth without an undue amount of experimentation.

Therefore, the instant specification does not provide enablement commensurate with the scope of the claim.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 98 and 218 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 98 and 218 are viewed as indefinite because they recite the limitation "said effective amount comprises about 0.01 mL to about 1 L of said formulation per nostril of said mammal." It is unclear how such large quantity of the formulation (1 liter is slightly more than quarter gallon) can be administered to nostril. Clarification is requested.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 70-75, 77, 88, 90-94, 104-108, 110-115, 119, 120, 143 and 145 are rejected under 35 U.S.C. 102(b) as being anticipated by Stankov (WO 96/00576).

WO 96/00576 is the PCT counterpart to US 5,880,101. WO 96/00576 is prior art under 35 USC §102(b) as a result of its January11, 1996 publication date. US 5,880,101 is not a prior art. Because WO 96/00576 and US 5,880,101 appear to have identical disclosures, the US patent is being used as a translation of WO patent. While any reference hereinafter to column and line numbers will be based upon the US patent disclosure, such reference should be interpreted as referring to the corresponding disclosure of the aforementioned PCT counterpart.

Stankov teaches treating patients having the symptoms of asthma, allergic rhinitis and sinusitis by daily oral administration of 1g of nystatin (or amphotericin) for 6 months. See col. 41, lines 5-17. The oral dose of the drug is in the range of 1-200 mg/kg body weight. See col. 38, lines 47-59. An almost complete disappearance of the symptoms was seen after 6-8 weeks

of therapy. See col. 41, lines 9-11. The allergies has resisted treatment for at least 5 years before the therapy. See col. 41, lines 7-9. Nystatin and amphotericin of Stankov are polyene macrolides. There antimycotic effect is believed to be based on interaction with the membrane-bound ergosterol of the fungi. See col. 2, lines 13-19.

Thus, Stankov teaches each and every limitation of Claims 70-75, 77, 88, 90-94, 104-108, 110-115, 119, 120, 143 and 145.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 78-87, 96-103, 109 and 116-118 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stankov.

Stankov applied as above. The reference further teaches that nystatin or amphotericin can be administered orally, topically or intranasally, e.g. as inhalation. See col. 38, lines 43-45. The oral dose of the drug is in the range of 1-200 mg/kg body weight and the frequency of application is 1-6 times per day, preferably 1-4 times per day. See col. 38, lines 47-59. The oral preparations include tablets, capsules, powder for emulsions, solutions and suspensions. See col. 38, lines 60-67. Aerosols and nasal sprays contain 2-200 μg/ml of the composition and may be administered 1-8 times per day. See col. 39, lines 16-21. With respect to Claim 103, Stankov teaches that their preparations include "at least one polyene macrolide", which

encompasses using both nystatin and amphotericin in the same preparation. See Abstract. Although Stankov does not explicitly teach the claimed mucoadministration of nystatin or amphotericin to the nasal-paranasal or lung airways for the treatment of asthma, allergic rhinitis and sinusitis, he fully discloses all the elements of the instant invention, i.e. (a) using nystatin or amphotericin for the treatment of asthma, allergic rhinitis and sinusitis, and (b) intranasal mode of administration. The selection of optimal mode, amount and frequency of administration of nystatin or amphotericin for the treatment of asthma, allergic rhinitis and sinusitis within the reference's generic disclosure, by routine experimentation, is obvious and within the skill of an ordinary practitioner. One of ordinary skill would have been motivated to do so with a reasonable expectation of success because the reference clearly teaches that nystatin and amphotericin "exhibit surprising therapeutical in vivo effects in a number of diseases when administered orally, intranasally or topically" at the claimed frequency and amounts.

12. Claims 76, 89, 122, 123, 127-129, 135-137, 144, 194-214 and 216-243 rejected under 35 U.S.C. 103(a) as being unpatentable over Stankov in view of Horner et al. ("Fungal Allergens", Clinical Microbiology Reviews, Apr. 1995, 161-179) and Bent III et al. ("Antifungal Activity Against Allergic Fungal Sinusitis Organisms", Laryngoscope, 106, 1996, pp. 1331-1334), both supplied by the Applicant.

Stankov teaches treating patients having allergies such as asthma, allergic rhinitis and sinusitis, by administration of nystatin or amphotericin as discussed above. Stankov teaches formulations, dosage, mode and frequency of administration as discussed above. Horner et al. teach that fungal spores "are universal atmospheric components indoors and outdoors and are

now generally recognized as important causes of respiratory allergies", including asthma and rhinitis. See p. 164. Stankov does not teach polyp formation or polypoid change as claimed in Claims 76 and 127. Further, Stankov does not teach the step of identifying a mammal having asthma and non-invasive fungus-induced rhinosinusitis as claimed in Claim 122 and those dependent thereon. However, Bent III et al. teach diagnostic criteria for AFS (aka non-invasive fungus-induced rhinosinusitis) including the presence of nasal polyps, fungal debris and eosinophilic mucus. See p. 1331. Further, Bent III et al. teach that diagnosis of AFS can be done by nasal examination. See p. 1333. Bent III et al. teach topical antifungal therapy of AFS by nasal postoperative irrigations. See entire document. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of treating allergic asthma, rhinitis and sinusitis of Stankov such that to include the step of identifying those patients that have fungal-induced rhinitis and sinusitis using the method described in Bent III et al. because of the widespread of fungal allergies as suggested by Horner et al. One having ordinary skill in the art would have been motivated to do this to obtain improved method of treatment of said fungal-induced rhinitis and sinusitis as suggested by Bent III et al.

With respect to Claims 89 and 209, Stankov does not teach the claimed azole compounds. However, Bent III et al. teach that ketaconazole was more effective than amphotericin and nystatin for the treatment of AFS. See p. 1333, Table III. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Stankov such that to employ ketaconazole in addition to or instead of nystatin or amphotericin for the treatment of asthma, allergic rhinitis and sinusitis.

One having ordinary skill in the art would have been motivated to do this because ketaconazole was shown to be more effective than nystatin or amphotericin in the treatment of AFS by Bent III et al.

13. Claims 95 and 215 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stankov either alone or in view of Bent III et al. and Horner et al. and further in view of either McCaffrey et al. (US 5,679,648) or Haria et al. ("Itraconazole. A reappraisal of its pharmacological properties and therapeutic use in the management of superficial fungal infections", Drugs, 51 (4), 585-620, Apr. 1996, Abstract), supplied by the Applicant.

Stankov either alone or in view of Bent III et al. and Horner et al. applied as above. With respect to Claims 95 and 215, Stankov does not teach the claimed itraconazole. However, Bent III et al. teach that itraconazole was almost as effective as nystatin in the treatment of AFS. See Table III. Further, both McCaffrey et al. and Haria et al. teach that itraconazole is less toxic than amphotericin. See McCaffrey et al. at col. 5, lines 1-6; Haria et al. at Abstract. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Stankov such that to employ itraconazole in addition to or instead of nystatin or amphotericin for the treatment of asthma, allergic rhinitis and sinusitis. One having ordinary skill in the art would have been motivated to do this because itraconazole was shown to be as effective as nystatin in the treatment of AFS by Bent III et al. and is less toxic than amphotericin as suggested by McCaffrey et al. or Haria et al.

Conclusion

14. No claim is allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Lamm whose telephone number is (703) 306-4541. The examiner can normally be reached on Monday to Friday from 9 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached at (703) 308-2927.

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

ml
11/26/03

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600